Image-Enhanced Endoscopy Is Critical in the Surveillance of Patients with Colonic IBD

Venkataraman Subramanian, MD, DM, MRCP(UK)[a,*],
Raf Bisschops, MD, PhD[b]

KEYWORDS

• Surveillance • Ulcerative colitis • Crohn's disease • Chromoendoscopy
• Narrow band imaging • Autofluorescence • FICE • iSCAN

KEY POINTS

- Cancer risk in patients with colonic inflammatory bowel disease (IBD) is high and increases over time. Quality and efficacy of surveillance is variable in routine clinical practice.
- Chromoendoscopy (CE) is recommended by most societies as the preferred test for colorectal cancer (CRC) surveillance in patients with colonic IBD. It has been shown unequivocally to improve dysplasia detection on targeted biopsies.
- Narrow band imaging has not shown superior dysplasia detected on targeted biopsies compared with CE or with white light imaging.

INTRODUCTION

Patients with IBD involving the colon have an increased risk for CRC compared with the general population.[1] Cancer in ulcerative colitis (UC) occurs at a younger age and increases with time, approaching 18% after 30 years of disease.[1] This increased risk has prompted both the North American and United Kingdom gastroenterology societies to recommend cancer prevention strategies.[2,3]

Disclosure Statement: V. Subramanian has no relevant disclosure to make; R. Bisschops is supported by a research grant from FWO-Vlaanderen. R. Bisschops received speaker's fees from Olympus, Pentax, and Fujifilm Corporation. Both authors contributed to the conception, drafting, critical revision, and final approval of the article.
[a] Molecular Gastroenterology, Leeds Institute of Biomedical and Clinical Sciences, St James University Hospital, University of Leeds, Leeds LS9 7TF, UK; [b] Department of Gastroenterology, University Hospital Leuven, Herestraat 49, 3000 Leuven, Belgium
* Corresponding author.
E-mail address: v.subramanian@leeds.ac.uk

Gastrointest Endoscopy Clin N Am 24 (2014) 393–403
http://dx.doi.org/10.1016/j.giec.2014.03.010
giendo.theclinics.com
1052-5157/14

Surveillance colonoscopies for early detection have been widely adopted to formally evaluate the benefits, risks, and costs of this approach.[4–7] Despite surveillance, interval cancer rates are high in these patients. A 2006 Cochrane review found no clear evidence that surveillance colonoscopy prolongs survival in patients with extensive colitis.[8] In the same year, a 30-year analysis of surveillance practice from St Mark's hospital reported that more than 50% of detected cancers were found to be interval cancers.[4] These data reflect an era when dysplasia was perceived to be invisible and only detected on random biopsies.[9]

In the past decade, endoscopic technology and technique has matured, with parallel evidence showing that the vast majority of dysplasia is visible and can be targeted. The long-term effects of surveillance using these new techniques, such as cancer-free survival, are still unknown. In this review, the authors summarize the existing literature on image-enhanced endoscopic techniques for surveillance of long-standing colonic IBD for the detection of dysplasia. They focus on dye-based chromoendoscopic techniques and present electronic-based image-enhanced endoscopic techniques such as narrow band imaging and autofluorescence endoscopy. Confocal laser endomicroscopy, a lesion characterization technology, is described in detail by Kiesslich and Matsumoto in another article in this issue.

SURVEILLANCE TECHNIQUES

Futility of White Light with Random Biopsy

Random mucosal sampling throughout the colon has historically been the mainstay of IBD surveillance colonoscopy. The technique is tedious, expensive, and time consuming, as it requires multiple biopsies to be taken segmentally throughout the colon and processed in separate jars. It has been estimated that at least 33 biopsies are needed to achieve 90% confidence to detect dysplasia if it is present.[10] The technique is not only inefficient but also inefficacious. The yield from random biopsy in studies on surveillance colonoscopy using high-definition (HD) endoscopes or other image-enhancement techniques is poor. **Table 1** summarizes the dysplasia yield from random biopsies for studies using image-enhanced endoscopic technologies.

The need to adopt image-enhanced techniques with targeted lesion detection is underscored by the low yield and unknown clinical significance from dysplasia found on random biopsies. Van den Broek and colleagues[20] published a retrospective analysis of the yield of dysplasia and clinical significance of dysplasia detected in random biopsies. Of 466 colonoscopies involving 167 patients done in a 10-year period from 1998 to 2008, dysplasia was detected by random biopsy only in 5 colonoscopies involving 4 patients. Only in one of these patients did protocolectomy confirm the presence of advanced neoplasia.

Superiority of Chromoendoscopy with Targeted Biopsy

The British Society of Gastroenterology[21] and the European Crohn's and Colitis organization[22] have specified chromoendoscopy (CE) as the preferred modality for surveillance in patients with colonic IBD. CE refers to the topical application of dyes (indigo carmine[23] or methylene blue[24]) to improve detection and delineation of surface abnormalities by pooling into mucosal crevices. Its application enhances the detection of subtle mucosal abnormalities to improve the yield of surveillance,[16] compared with white light inspection alone. Both indigo carmine and methylene blue have been widely used and shown to be effective. CE was first shown to be useful in the detection of flat adenomas in the sporadic setting and in patients with familial polyposis

Table 1
Yield of dysplasia from random biopsies in prospective endoscopic studies involving surveillance colonoscopy with image-enhanced endoscopy for colonic IBD in the last 10 years

Study Author, Year	Country	Image-Enhanced Modality Used	Number of Patients	Number of Random Biopsies with Dysplasia	Total Number of Random Biopsies	Mean Number of Random Biopsies per Episode of Dysplasia
Kiesslich et al,[11] 2003	Germany	Methylene blue chromoendoscopy	165	2 (in white light arm only)	5098	2549
Matsumoto et al,[12] 2003	Japan	Indigo carmine chromoendoscopy	57	3	702	234
Rutter et al,[13] 2004	United Kingdom	Indigo carmine chromoendoscopy	100	0	2904	—
Kiesslich et al,[14] 2007	Germany	Methylene blue chromoendoscopy	153	2 (in white light arm only)	2854	1427
Dekker et al,[15] 2007	Netherlands	Narrow Band Imaging (first generation)	42	1	1522	1522
Van den Broek et al,[16] 2008	Netherlands	Autofluorescence endoscopy	50	2	1992	996
Marion et al,[17] 2008	USA	Methylene blue chromoendoscopy	102	3	3264	1088
Van den Broek et al,[18] 2011	Netherlands	Narrow Band Imaging (second generation)	48	3	1580	527
Ignjatovic et al,[19] 2012	United Kingdom	Narrow Band Imaging (second generation)	112	1	2707	2707

syndromes[25,26]; during the past decade, studies have also shown CE to augment the visualization of dysplasia in UC.[27,28]

Table 2 lists the published studies comparing pancolonic CE with WLE for detection of dysplasia in colonic IBD. A meta-analysis of the available data in 2011[32] and an updated one in 2013[33] that included 6 studies with 665 patients confirmed the superiority of CE with targeted biopsy to standard WLE with random biopsy. A 6% increase in the yield of dysplasia was noted in the most recent analysis, leading to a number needed to treat of 16 to detect an additional patient with dysplasia if using CE with targeted biopsy. Compared with white light, the use of CE added almost 11 minutes to the total procedure time, which also included the time spent on random biopsies.

Improvements in detection and visualization of dysplasia in patients with IBD have led to an increase in their local endoscopic resection, without the need for colectomy,[34] all emphasizing the importance of careful and complete surveillance colonoscopies in these high-risk patients. Although CE is increasingly recommended for this purpose,[35,36] it has yet to be widely adopted as standard of care in clinical practice. Some of the reasons for this may be because CE is perceived as time consuming and often messy. These and perhaps additional factors like differences in application technique (spray catheter vs foot pump), dye contact time, operator experience, and interpretation of staining are the important training ingredients to broadly implement CE into routine clinical practice. Picco and colleagues[31] have shown excellent interobserver agreement among nonexpert endoscopists in the detection and interpretation of lesions detected by CE and the suggested steps toward training a unit to implement CE.

High-Definition Electronic Image-Enhanced Endoscopy (Virtual Chromoendoscopy)

CE with indigo carmine or methylene blue has been well demonstrated and is now incorporated into surveillance guidelines.[21] However, the perceived increased effort, skill, time, and cost of CE have motivated studies on electronic-based image-enhanced endoscopy or dyeless virtual CE. Three different systems are commercially available: Narrow Band imaging (NBI, Olympus, Tokyo, Japan), Fujinon Intelligent Color Enhancement (FICE, Fujifilm, Tokyo, Japan), and i-scan (Pentax, Tokyo, Japan). The basic principle of all these enhancement techniques is to filter the classical white light images to enhance superficial structural and vascular changes in the mucosa. In case of NBI, an optical filter is placed in front of the excitation white light source to narrow the wavelength to 30-nm bandwidths in the blue (415 nm) and green (540 nm) regions of the spectrum. Superficial mucosal structures (pit patterns) and microvasculature are enhanced using a narrow band light because it has more shallow tissue penetration and is mostly absorbed by hemoglobin in the vessels.

In contrast to NBI, the FICE and i-scan techniques do not use a physical filter but a postprocessing spectrum analysis software to enhance the image features and characteristics. The video processor disintegrates the different red green blue components of the white light image. Each component is then independently converted along its tone curve, followed by resynthesis of the 3 components to reconstruct a new digital image.[37–41] In theory, the number of possible combinations is endless, but each system comes with readily available filters. For example, the FICE system has 10 available filters, which can be activated by a push of the button and can be changed on the numeric key path of the processor's keyboard. Pentax has 3 major i-scan presets with standardized surface, tone, and contrast enhancement that come as a factory setting.

Because all these techniques are standardly available and can be simply activated by pushing a button, they have the appeal to overcome the technical drawbacks of

Table 2
Published studies comparing pancolonic chromoendoscopy with white light endoscopy in detection of dysplastic lesions for surveillance colonoscopy in long-standing colonic IBD

Author, Year	Country	No. of Endoscopists	Dye	Study Design	Inclusion Criteria	No. of Patients	No. with Dysplasia	Was CE Better[a]
Kiesslich et al,[11] 2003	Germany	Multiple	MB	Randomized 1:1	Long-standing UC ≥8 y	165	18	Y
Matsumoto et al,[12] 2003	Japan	Single	IC	Prospective cohort, WLE followed by CE	Pancolitis >5 y	57	12	Y
Rutter et al,[13] 2004	UK	Single	IC	Prospective cohort, WLE followed by CE	Long-standing extensive UC	100	7	Y
Kiesslich et al,[14] 2007	Germany	Multiple	MB	Randomized 1:1	Long-standing UC ≥8 y	153	15	Y
Marion et al,[17] 2008	USA	Multiple	MB	Prospective cohort, WLE followed by CE	Extensive UC or Crohn's colitis involving >1/3 of colon	102	22	Y
Günther et al,[29] 2011	Germany	Multiple	IC	Subdivided retrospectively into 50 patients in each group	Extensive UC >8 y or colonic Crohn's colitis >10 y	100	2	N
Hlavaty et al,[30] 2011	Slovakia	Multiple	IC	Retrospective analysis based on consent for WLE alone or WLE followed by CE	Pancolitis >8 y or left sided colitis >15 y	45	6	Y
Picco et al,[31] 2013	USA	Multiple	IC	Prospective cohort WLE followed by CE	Long standing extensive UC >8 y	75	16	Y

Abbreviations: IC, indigo carmine; MB, methylene blue; N, no; Y, yes.
[a] Detection by CE was significantly ($P<.05$) better than by WLE.

dye-based CE. In non-IBD settings, the diagnostic accuracy of NBI, FICE, and i-scan in discriminating neoplastic from nonneoplastic lesions is comparable to dye-based CE,[42–46] and at least this aspect of the technique seems to have a short learning curve.[47,48]

To date, the only electronic image-enhanced endoscopic technique to be assessed for diagnostic accuracy in IBD, however, has been using NBI. Five randomized trials[15,18,19,49,50] using NBI compared with CE ($n = 2$) or white light imaging ($n = 3$) did not show superiority in the detection of neoplastic lesions in long-standing colitis. Dekker and colleagues[15] showed no diagnostic advantage in a tandem colonoscopic study that compared the first-generation NBI system to standard-resolution WLE for the detection of colitis-associated neoplasia. NBI detected 52 visible lesions in 17 patients (8 neoplastic), compared with 28 visible lesions in 13 patients (7 neoplastic) during WLE inspection. Two more trials comparing HD-NBI to WLE also found no significant difference in the detection of neoplastic lesions when using NBI. Van den Broek and colleagues[18] performed a tandem colonoscopy study and found 13 of 16 (81%) neoplastic lesions using HD-NBI compared with 11 of 16 (69%) neoplastic lesions using HD-WLE.[18] Random biopsy protocol yielded no significant additional neoplasia; in a total of 1590 random biopsies, 3 demonstrated low-grade dysplasia of which 2 were found in the proximity of dysplasia associated lesion or mass lesions. Ignjatovic and colleagues[19] assessed the diagnostic yield of HD-NBI compared with WLE in a randomized controlled trial without back-to-back design and could not find a significant difference in neoplasia detection between the 2 techniques (5 neoplastic lesions in 5 patients for HD-NBI vs 7 neoplastic lesions in 5 patients for HD-WLE). Only 1 in 2707 random biopsies yielded an additional diagnosis of low-grade dysplasia in a patient who already had a lesion detected by NBI-targeted biopsies.[19] These studies add further to the evidence random biopsies are low yield and should be abandoned.[18,19,51]

Two trials have compared HD-NBI to CE. In a back-to-back study,[49] 33 patients underwent HD colonoscopy with NBI followed by CE (0.5% indigo carmine) and 27 patients were randomized to the opposite sequence to assess miss rates of the 2 techniques. The study showed a nonsignificant trend toward a higher miss rate using NBI. In the NBI first group, NBI detected 7 neoplastic lesions in 4 patients during the first pass and CE detected 5 additional lesions in 4 patients during the second pass. In the HD-CE first group, CE detected 5 neoplastic lesions in 4 patients during the first pass and NBI detected 3 neoplastic lesions in 1 patient during the second pass. The withdrawal time for CE was significantly longer (26.87 $\pm$ 9.89 minutes for CE vs 15.74 $\pm$ 5.62 minutes for NBI, $P<.01$).[49] Preliminary abstract data of a randomized trial comparing HD-NBI with CE (0.1% methylene blue) showed no significant difference in neoplasia detection rates between either modalities (18.5% for HD-NBI and 16.7% for HD-CE, $P = .658$).[50]

At present, CE remains the gold standard for colitis surveillance. Further studies assessing NBI or other electronic image-enhanced endoscopic methods compared with CE are necessary before any change in recommendations or clinical practice.

Autofluorescence Imaging

Autofluorescence imaging (AFI) is a novel imaging technique. AFI is available on the monochrome chip (Lucera, Olympus, Tokyo, Japan), which has 2 charge-coupled devices for WLE and AFI and can be activated by a push of the button. An ultraviolet filter is placed in front of the light source. All tissues exhibit autofluorescence when excited by ultraviolet (>400 nm) or short visible light (400–550 nm). Autofluorescence is generated by fluorophores, certain biomolecules (collagen, elastin), emitting a longer

wavelength than the excitation light. AFI is influenced by several factors, including tissue architecture (mucosal thickening), light absorption and scattering properties (mainly determined by the absorptive capacity of hemoglobin in neoplastic neovascularization), the biochemical content (concentration of fluorophores), and metabolic status of the tissue.[52–59] Using AFI, neoplastic tissue is visible as a purple lesion on a greenish background fluorescence of normal colonic tissue. AFI has therefore the potential to serve as a red flag technique highlighting even very early minute neoplastic changes in the colonic mucosa. In contrast to NBI, the available data on AFI for colitis surveillance is sparse. In a single prospective randomized crossover trial comparing the neoplasia detection of WLE with that of AFI targeted biopsies, Van den Broek and colleagues[16] found a significant higher yield for AFI. In the AFI first group, 10 lesions in 25 patients were detected and subsequent WLE did not detect any additional lesions. However, in the WLE first group, 3 neoplastic lesions were detected in 25 patients, but AFI additionally detected 3 lesions. This resulted in a significantly different miss rate (50% vs 0, $P = .036$) between the 2 techniques.[16] Further larger trials are needed to confirm the potential of this red flag technique and to compare its yield with that of CE-guided biopsies.

SUMMARY

Patients with long-standing extensive colitis are at increased risk for developing neoplasia and the literature suggests that surveillance endoscopy reduces mortality from CRC in these patients. CE with indigo carmine or methylene blue has replaced random biopsies as a standard for surveillance in these patients; this is supported by several clinical trials and incorporated in recent guidelines. Future studies on digitally enhanced imaging, such as NBI, will continue to be of interest, but one has to be cautious that current data do not show their superiority compared with CE.

Future unmet needs in colitis surveillance include proper training and implementation for all endoscopists. Although the evidence is abundant and supports the use of CE, it is far from being widely implemented outside of tertiary referral centers. The minimal criteria need to be standardized to determine properly trained endoscopists. An endoscopist may need to start with CE coupled with 4-quadrant biopsies and then cautiously proceed with CE-guided biopsies once competence metrics are met. The implementation of these techniques needs to be monitored in prospective quality registries to ensure patient safety and the performance by secondary care gastroenterologists.

REFERENCES

1. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 2001;48:526–35.
2. Carter MJ, Lobo AJ, Travis SP. Guidelines for the management of inflammatory bowel disease in adults. Gut 2004;53(Suppl 5):V1–16.
3. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol 2004;99:1371–85.
4. Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology 2006;130:1030–8.
5. Delaunoit T, Limburg PJ, Goldberg RM, et al. Colorectal cancer prognosis among patients with inflammatory bowel disease. Clin Gastroenterol Hepatol 2006;4:335–42.

6. Lakatos L, Mester G, Erdelyi Z, et al. Risk factors for ulcerative colitis-associated colorectal cancer in a Hungarian cohort of patients with ulcerative colitis: results of a population-based study. Inflamm Bowel Dis 2006;12:205–11.
7. Choi PM, Nugent FW, Schoetz DJ Jr, et al. Colonoscopic surveillance reduces mortality from colorectal cancer in ulcerative colitis. Gastroenterology 1993; 105:418–24.
8. Collins PD, Mpofu C, Watson AJ, et al. Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease. Cochrane Database Syst Rev 2006;(2):CD000279.
9. Eaden JA, Ward BA, Mayberry JF. How gastroenterologists screen for colonic cancer in ulcerative colitis: an analysis of performance. Gastrointest Endosc 2000;51:123–8.
10. Rubin CE, Haggitt RC, Burmer GC, et al. DNA aneuploidy in colonic biopsies predicts future development of dysplasia in ulcerative colitis. Gastroenterology 1992;103:1611–20.
11. Kiesslich R, Fritsch J, Holtmann M, et al. Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. Gastroenterology 2003;124:880–8.
12. Matsumoto T, Nakamura S, Jo Y, et al. Chromoscopy might improve diagnostic accuracy in cancer surveillance for ulcerative colitis. Am J Gastroenterol 2003; 98:1827–33.
13. Rutter MD, Saunders BP, Schofield G, et al. Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. Gut 2004;53:256–60.
14. Kiesslich R, Goetz M, Lammersdorf K, et al. Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. Gastroenterology 2007;132:874–82.
15. Dekker E, van den Broek FJ, Reitsma JB, et al. Narrow-band imaging compared with conventional colonoscopy for the detection of dysplasia in patients with longstanding ulcerative colitis. Endoscopy 2007;39:216–21.
16. van den Broek FJC, Fockens P, van Eeden S, et al. Endoscopic tri-modal imaging for surveillance in ulcerative colitis: randomised comparison of high-resolution endoscopy and autofluorescence imaging for neoplasia detection; and evaluation of narrow-band imaging for classification of lesions. Gut 2008; 57:1083–9.
17. Marion JF, Waye JD, Present DH, et al. Chromoendoscopy-targeted biopsies are superior to standard colonoscopic surveillance for detecting dysplasia in inflammatory bowel disease patients: a prospective endoscopic trial. Am J Gastroenterol 2008;103:2342–9.
18. van den Broek FJC, Fockens P, van Eeden S, et al. Narrow-band imaging versus high-definition endoscopy for the diagnosis of neoplasia in ulcerative colitis. Endoscopy 2011;43:108–15.
19. Ignjatovic A, East JE, Subramanian V, et al. Narrow band imaging for detection of dysplasia in colitis: a randomized controlled trial. Am J Gastroenterol 2012; 107:885–90.
20. van den Broek FJ, Stokkers PC, Reitsma JB, et al. Random biopsies taken during colonoscopic surveillance of patients with longstanding ulcerative colitis: low yield and absence of clinical consequences. Am J Gastroenterol 2011. [Epub ahead of print].
21. Cairns SR, Scholefield JH, Steele RJ, et al. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). Gut 2010;59:666–89.

22. Annese V, Daperno M, Rutter MD, et al. European evidence based consensus for endoscopy in inflammatory bowel disease. J Crohns Colitis 2013;7:982–1018.
23. Olliver JR, Wild CP, Sahay P, et al. Chromoendoscopy with methylene blue and associated DNA damage in Barrett's oesophagus. Lancet 2003;362:373–4.
24. Davies J, Burke D, Olliver JR, et al. Methylene blue but not indigo carmine causes DNA damage to colonocytes in vitro and in vivo at concentrations used in clinical chromoendoscopy. Gut 2007;56:155–6.
25. Huneburg R, Lammert F, Rabe C, et al. Chromocolonoscopy detects more adenomas than white light colonoscopy or narrow band imaging colonoscopy in hereditary nonpolyposis colorectal cancer screening. Endoscopy 2009;41:316–22.
26. Le Rhun M, Coron E, Parlier D, et al. High resolution colonoscopy with chromoscopy versus standard colonoscopy for the detection of colonic neoplasia: a randomized study. Clin Gastroenterol Hepatol 2006;4:349–54.
27. Rubin DT, Rothe JA, Hetzel JT, et al. Are dysplasia and colorectal cancer endoscopically visible in patients with ulcerative colitis? Gastrointest Endosc 2007;65:998–1004.
28. Rutter MD, Saunders BP, Wilkinson KH, et al. Most dysplasia in ulcerative colitis is visible at colonoscopy. Gastrointest Endosc 2004;60:334–9.
29. Günther U, Kusch D, Heller F, et al. Surveillance colonoscopy in patients with inflammatory bowel disease: comparison of random biopsy vs. targeted biopsy protocols. Int J Colorectal Dis 2011;26:667–72.
30. Hlavaty T, Huorka M, Koller T, et al. Colorectal cancer screening in patients with ulcerative and Crohn's colitis with use of colonoscopy, chromoendoscopy and confocal endomicroscopy. Eur J Gastroenterol Hepatol 2011;23:680–9.
31. Picco MF, Pasha S, Leighton JA, et al. Procedure time and the determination of polypoid abnormalities with experience: implementation of a chromoendoscopy program for surveillance colonoscopy for ulcerative colitis. Inflamm Bowel Dis 2013;19:1913–20.
32. Subramanian V, Mannath J, Ragunath K, et al. Meta-analysis: the diagnostic yield of chromoendoscopy for detecting dysplasia in patients with colonic inflammatory bowel disease. Aliment Pharmacol Ther 2011;33:304–12.
33. Soetikno R, Subramanian V, Kaltenbach T, et al. The detection of nonpolypoid (flat and depressed) colorectal neoplasms in patients with inflammatory bowel disease. Gastroenterology 2013;144:1349–52, 1352.
34. Hurlstone DP, Sanders DS, Atkinson R, et al. Endoscopic mucosal resection for flat neoplasia in chronic ulcerative colitis: can we change the endoscopic management paradigm? Gut 2007;56:838–46.
35. Itzkowitz SH, Harpaz N. Diagnosis and management of dysplasia in patients with inflammatory bowel diseases. Gastroenterology 2004;126:1634–48.
36. Hayashi N, Tanaka S, Hewett DG, et al. Endoscopic prediction of deep submucosal invasive carcinoma: validation of the narrow-band imaging international colorectal endoscopic (NICE) classification. Gastrointest Endosc 2013;78:625–32.
37. Kodashima S, Fujishiro M. Novel image-enhanced endoscopy with i-scan technology. World J Gastroenterol 2010;16:1043–9.
38. Adler A, Aschenbeck J, Yenerim T, et al. Narrow-band versus white-light high definition television endoscopic imaging for screening colonoscopy: a prospective randomized trial. Gastroenterology 2009;136:410–6.

39. Hoffman A, Sar F, Goetz M, et al. High definition colonoscopy combined with i-Scan is superior in the detection of colorectal neoplasias compared with standard video colonoscopy: a prospective randomized controlled trial. Endoscopy 2010;42(10):827–33.
40. Hoffman A, Kagel C, Goetz M, et al. Recognition and characterization of small colonic neoplasia with high-definition colonoscopy using i-Scan is as precise as chromoendoscopy. Dig Liver Dis 2010;42(1):45–50.
41. Rex DK, Helbig CC. High yields of small and flat adenomas with high-definition colonoscopes using either white light or narrow band imaging. Gastroenterology 2007;133(1):42–7.
42. Hewett DG, Kaltenbach T, Sano Y, et al. Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging. Gastroenterology 2012;143:599–607.
43. Basford PJ, Longcroft-Wheaton G, Higgins B, et al. High-definition endoscopy with i-Scan for evaluation of small colon polyps: the HiSCOPE study. Gastrointest Endosc 2014;79:111–8.
44. Longcroft-Wheaton G, Brown J, Cowlishaw D, et al. High-definition vs standard-definition colonoscopy in the characterization of small colonic polyps: results from a randomized trial. Endoscopy 2012;44:905–10.
45. Longcroft-Wheaton GR, Higgins B, Bhandari P. Flexible spectral imaging color enhancement and indigo carmine in neoplasia diagnosis during colonoscopy: a large prospective UK series. Eur J Gastroenterol Hepatol 2011;23:903–11.
46. Pohl J, Nguyen-Tat M, Pech O, et al. Computed virtual chromoendoscopy for classification of small colorectal lesions: a prospective comparative study. Am J Gastroenterol 2008;103:562–9.
47. Bouwens MW, de RR, Masclee AA, et al. Optical diagnosis of colorectal polyps using high-definition i-scan: an educational experience. World J Gastroenterol 2013;19:4334–43.
48. Neumann H, Vieth M, Fry LC, et al. Learning curve of virtual chromoendoscopy for the prediction of hyperplastic and adenomatous colorectal lesions: a prospective 2-center study. Gastrointest Endosc 2013;78(1):115–20.
49. Pellisé M, López-Cerón M, Rodríguez de Miguel C, et al. Narrow-band imaging as an alternative to chromoendoscopy for the detection of dysplasia in long-standing inflammatory bowel disease: a prospective, randomized, crossover study. Gastrointest Endosc 2011;74:840–8.
50. Bisschops R, Bessissow T, Baert FJ, et al. Chromo-endoscopy versus narrow band imaging in ulcerative colitis: a prospective randomized controlled trial. Gastrointest Endosc 2012;44:AB148.
51. Subramanian V, Ramappa V, Telakis E, et al. Comparison of high definition with standard white light endoscopy for detection of dysplastic lesions during surveillance colonoscopy in patients with inflammatory bowel disease. Inflamm Bowel Dis 2013;19:350–5.
52. DaCosta RS, Andersson H, Wilson BC. Molecular fluorescence excitation-emission matrices relevant to tissue spectroscopy. Photochem Photobiol 2003;78:384–92.
53. DaCosta RS, Wilson BC, Marcon NE. Optical techniques for the endoscopic detection of dysplastic colonic lesions. Curr Opin Gastroenterol 2005;21(1):70–9.
54. Matsumoto T, Nakamura S, Moriyama T, et al. Autofluorescence imaging colonoscopy for the detection of dysplastic lesions in ulcerative colitis: a pilot study. Colorectal Dis 2010;12:e291–7.

55. Bessissow T, Bisschops R. Advanced endoscopic imaging for dysplasia surveillance in ulcerative colitis. Expert Rev Gastroenterol Hepatol 2013;7:57–67.
56. Neumann H, Neurath MF, Mudter J. New endoscopic approaches in IBD. World J Gastroenterol 2011;17(1):63–8.
57. Subramanian V, Ragunath K. Advanced endoscopic imaging: a review of commercially available technologies. Clin Gastroenterol Hepatol 2014;12:368–76.e1 pii:S1542–3565(13)00878-1.
58. van den Broek FJ, van Es JA, van Eeden S, et al. Pilot study of probe-based confocal laser endomicroscopy during colonoscopic surveillance of patients with longstanding ulcerative colitis. Endoscopy 2011;43:116–22.
59. Jess T, Loftus EV Jr, Velayos FS, et al. Incidence and prognosis of colorectal dysplasia in inflammatory bowel disease: a population-based study from Olmsted County, Minnesota. Inflamm Bowel Dis 2006;12(8):669–76.